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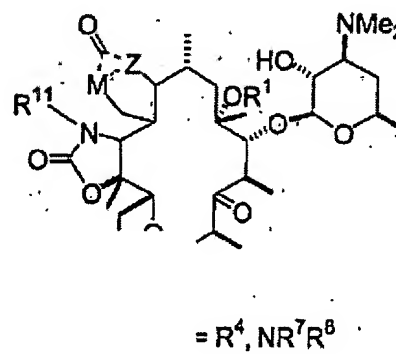
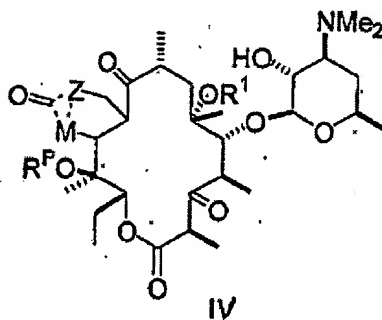
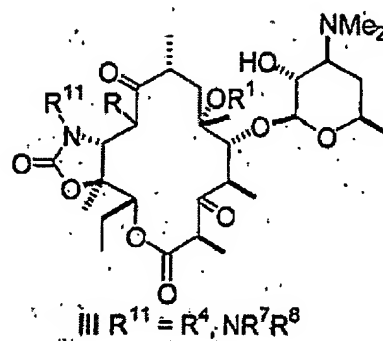
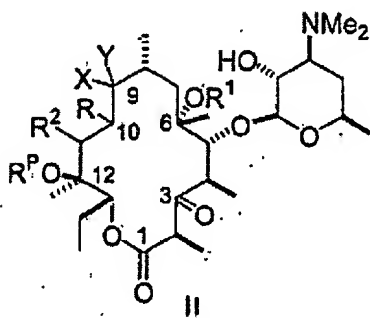
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JC17 Rec'd PCT/PTO 20 JUN 2005

IN THE CLAIMS:

1. (Currently Amended) A 10-desmethyl macrolide comprising a 10-position substituent, wherein the 10-desmethyl macrolide comprises a saturated  $C_{13}ON_x$  lactone ring substituted by one or more sugars, having no  $CH_3$  at the 10-position carbon, and wherein x is 0 or 1.
2. (Currently Amended) The 10-desmethyl macrolides of claim 1, wherein the 10-position substituent comprises a carbon which is attached to the 10-position carbon of the macrolide lactone ring.
3. (Currently Amended) The 10-desmethyl macrolide of claim 1, wherein the 10-position substituent is methylene, substituted methyl, or CHO.
4. (Currently Amended) The 10-desmethyl macrolide of claim 3, wherein the 10-position substituent comprises an aryl group.
5. (Currently Amended) The macrolide of claim 1, wherein the macrolide is substituted in the 2-position by methyl and hydrogen or fluorine; in the 3-position by oxo or optionally substituted hydroxy; in the 4-position by methyl; in the 5-position by an oxygen-attached desosamine; in the 6-position by methyl and an optionally substituted hydroxyl; in the 8-position by methyl and hydrogen or fluorine; in the 9-position by oxo; in the 10-position by methylene, CHO, substituted methyl, or carboxy or substituted carboxy; in the 11- and 12-positions by a group forming a fused ring at the 11, 12 and optionally 10-positions; at the 12-position additionally by a methyl group; and at the 13-position by an ethyl group.

6. Macrolides as claimed in claim 1 of formula II, III, IV or V



- (1) R is methyl substituted with one or more substituents selected from the group consisting of
- (i) CN,
  - (ii) F,
  - (iii)  $\text{CO}_2\text{R}^3$  wherein  $\text{R}^3$  is selected from hydrogen,  $\text{C}_1$ - $\text{C}_3$ -alkyl or aryl substituted  $\text{C}_1$ - $\text{C}_3$ -alkyl, or heteroaryl substituted  $\text{C}_1$ - $\text{C}_3$ -alkyl,
  - (iv)  $\text{OR}^4$  wherein  $\text{R}^4$  is selected from hydrogen,  $\text{C}_1$ - $\text{C}_4$ -alkyl or aryl substituted  $\text{C}_1$ - $\text{C}_4$ -alkyl, or heteroaryl substituted  $\text{C}_1$ - $\text{C}_4$ -alkyl, heterocycloalkyl and optionally substituted cycloalkyl,  $\text{C}_1$ - $\text{C}_3$ -alkoxy- $\text{C}_1$ - $\text{C}_3$ -alkoxy,  $\text{C}_2$ - $\text{C}_4$ -alkenyl or aryl substituted  $\text{C}_2$ - $\text{C}_4$ -alkenyl, or heteroaryl substituted  $\text{C}_2$ - $\text{C}_4$ -alkenyl, heterocycloalkyl and optionally substituted cycloalkyl, aryl or optionally substituted aryl, heteroaryl or optionally substituted heteroaryl,
  - (v)  $\text{S(O)}_n\text{R}^3$  wherein  $n=0, 1$  or  $2$  and  $\text{R}^3$  is as previously defined
  - (vi)  $\text{NR}^4\text{C(O)R}^3$  wherein  $\text{R}^3$  and  $\text{R}^4$  are as previously defined
  - (vii)  $\text{NR}^4\text{C(O)NR}^5\text{R}^6$  wherein  $\text{R}^4$  is defined as defined previously, and  $\text{R}^5$  and  $\text{R}^6$  are independently selected from hydrogen,  $\text{C}_1$ - $\text{C}_3$ -alkyl,  $\text{C}_1$ - $\text{C}_3$  alkyl substituted with aryl, substituted aryl, heteroaryl, substituted heteroaryl
  - (viii)  $\text{NR}^7\text{R}^8$  wherein  $\text{R}^7$  and  $\text{R}^8$  are independently selected from the group consisting of
    - (a) hydrogen
    - (b)  $\text{C}_1$ - $\text{C}_{12}$ -alkyl, and optionally substituted  $\text{C}_1$ - $\text{C}_{12}$ -alkyl
    - (c)  $\text{C}_2$ - $\text{C}_{12}$ -alkenyl, and optionally substituted  $\text{C}_2$ - $\text{C}_{12}$ -alkenyl
    - (d)  $\text{C}_2$ - $\text{C}_{12}$ -alkynyl, and optionally substituted  $\text{C}_2$ - $\text{C}_{12}$ -alkynyl
    - (e) aryl, and optionally substituted aryl
    - (f) heteroaryl, and optionally substituted heteroaryl
    - (g) heterocycloalkyl, and optionally substituted heterocycloalkyl
    - (h)  $\text{C}_1$ - $\text{C}_{12}$  alkyl substituted with aryl, and optionally substituted with substituted aryl
    - (i)  $\text{C}_1$ - $\text{C}_{12}$  alkyl substituted with heteroaryl, and optionally substituted with substituted heteroaryl
    - (j)  $\text{C}_1$ - $\text{C}_{12}$  alkyl substituted with heterocycloalkyl, and with optionally substituted heterocycloalkyl, and
    - (k)  $\text{R}^7$  and  $\text{R}^8$  taken together with the atom to which they are attached from a 3-10-membered heterocycloalkyl ring which may contain one or more additional heteroatoms and may be substituted with one or more substituents independently selected from the group consisting of

- (aa) halogen, hydroxy, C<sub>1</sub>-C<sub>3</sub>-alkoxy, alkoxy-C<sub>1</sub>-C<sub>3</sub>- alkoxy, oxo, C<sub>1</sub>-C<sub>3</sub>-alkyl, aryl and optionally substituted aryl, heteroaryl and optional substituted heteroaryl
- (bb) CO<sub>2</sub>R<sup>3</sup> wherein R<sup>3</sup> is as previously defined, and
- (cc) C(O)NR<sup>5</sup>R<sup>6</sup> wherein R<sup>5</sup> and R<sup>6</sup> are as previously defined,
- (ix) aryl, and optionally substituted aryl, and
- (x) heteroaryl, and optionally substituted heteroaryl,
- (2) C<sub>2</sub>-C<sub>10</sub>-alkyl,
- (3) C<sub>2</sub>-C<sub>10</sub>-alkyl substituted with one or more substituents selected from the group consisting of
  - (i) halogen,
  - (ii) OR<sup>4</sup> wherein R<sup>4</sup> is as defined previously
  - (iii)-CHO,
  - (iv) oxo,
  - (v) NR<sup>7</sup>R<sup>8</sup> wherein R<sup>7</sup> and R<sup>8</sup> are defined as previously
  - (vi) =N-O-R<sup>4</sup> is wherein R<sup>3</sup> is as previously defined
  - (vii)-CN
  - (viii)-S(O)<sub>n</sub>R<sup>3</sup> wherein n = 0, 1 or 2 and R<sup>3</sup> is as previously defined
  - (ix) aryl, and optionally substituted aryl
  - (x) heteroaryl, and optionally substituted heteroaryl
  - (xi) C<sub>3</sub>-C<sub>8</sub>-cycloalkyl, and optionally substituted C<sub>3</sub>-C<sub>8</sub>-cycloalkyl
  - (xii) heterocycloalkyl, and optionally substituted heterocycloalkyl
  - (xiii) NR<sup>4</sup>C(O)R<sup>3</sup> where R<sup>3</sup> and R<sup>4</sup> are as previously defined
  - (xiv) NR<sup>4</sup>C(O)NR<sup>5</sup>R<sup>6</sup> wherein R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are as previously defined
  - (xv) =N-NR<sup>7</sup>R<sup>8</sup> wherein R<sup>7</sup> and R<sup>8</sup> are as previously defined
  - (xvi)=N-R<sup>4</sup> wherein R<sup>4</sup> is as previously defined
  - (xvii)=N-NR<sup>4</sup>C(O)R<sup>3</sup> wherein R<sup>3</sup> and R<sup>4</sup> are as previously defined, and
  - (xviii)=N-NR<sup>4</sup>C(O)NR<sup>5</sup>R<sup>6</sup> wherein R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are as previously defined,
- (4) C<sub>2</sub>-C<sub>10</sub>-alkenyl,
- (5) C<sub>2</sub>-C<sub>10</sub>-alkenyl substituted with one or more substituents selected from the group consisting of
  - (i) halogen,
  - (ii) OR<sup>4</sup> wherein R<sup>4</sup> is as previously defined
  - (iii) O-S(O)<sub>n</sub>R<sup>3</sup> where n and R<sup>3</sup> are as previously defined
  - (iv)-CHO,
  - (v) oxo,

- (vi)-CO<sub>2</sub>R<sup>3</sup> where R<sup>3</sup> is as previously defined
- (vii)-C(O)-R<sup>4</sup> where R<sup>4</sup> is as previously defined
- (viii) -CN
- (ix) aryl, and optionally substituted aryl
- (x) heteroaryl, and optionally substituted heteroaryl
- (xi) C<sub>3</sub>-C<sub>7</sub>-cycloalkyl
- (xii) C<sub>1</sub>-C<sub>12</sub>-alkyl substituted with heteroaryl
- (xiii)NR<sup>7</sup>R<sup>8</sup> wherein R<sup>7</sup> and R<sup>8</sup> are as previously defined
- (xiv) NR<sup>4</sup>C(O)R<sup>3</sup> where R<sup>3</sup> and R<sup>4</sup> are as previously defined
- (xv) NR<sup>4</sup>C(O)NR<sup>5</sup>R<sup>6</sup> where R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are as previously defined
- (xvi) =N-O-R<sup>4</sup> where R<sup>4</sup> is as previously defined
- (xvii)=N-NR<sup>7</sup>R<sup>8</sup> wherein R<sup>7</sup> and R<sup>8</sup> are as previously defined
- (xviii) =N-NR<sup>4</sup> wherein R<sup>4</sup> is as previously defined
- (xix)=N-NR<sup>4</sup>C(O)R<sup>3</sup> wherein R<sup>3</sup> and R<sup>4</sup> are as previously defined, and
- (xx)=N-NR<sup>4</sup>C(O)NR<sup>5</sup>R<sup>6</sup> wherein R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are as previously defined,
- (6) C<sub>2</sub>-C<sub>10</sub>-alkynyl
- (7) C<sub>2</sub>-C<sub>10</sub>-alkynyl substituted with one or more substituents selected from the group consisting of
  - (i) trialkylsilyl
  - (ii) halogen,
  - (iii) -CN
  - (iv) OR<sup>4</sup> where R<sup>4</sup> is defined as previously
  - (v)-CHO,
  - (vi) oxo,
  - (vii)-CO<sub>2</sub>R<sup>3</sup> where R<sup>3</sup> is as previously defined
  - (viii)-C(O)NR<sup>5</sup>R<sup>6</sup> wherein R<sup>5</sup> and R<sup>6</sup> are as previously defined
  - (ix)NR<sup>7</sup>R<sup>8</sup> wherein R<sup>7</sup> and R<sup>8</sup> are as previously defined
  - (x) O-S(O)<sub>n</sub>R<sup>3</sup> where n and R<sup>3</sup> are as previously defined
  - (xi) C<sub>3</sub>-C<sub>7</sub>-cycloalkyl
  - (xii) C<sub>1</sub>-C<sub>12</sub>-alkyl substituted with heteroaryl
  - (xiii)aryl, and optionally substituted aryl
  - (xiv) heteroaryl, and optionally substituted heteroaryl
  - (xv) NR<sup>4</sup>C(O)R<sup>3</sup> where R<sup>3</sup> and R<sup>4</sup> are as previously defined
  - (xvi) NR<sup>4</sup>C(O)NR<sup>5</sup>R<sup>6</sup> where R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are as previously defined
  - (xvii) =N-O-R<sup>4</sup> where R<sup>4</sup> is as previously defined
  - (xviii)=N-NR<sup>7</sup>R<sup>8</sup> wherein R<sup>7</sup> and R<sup>8</sup> are as previously defined

(xix)  $=N-NR^4C(O)R^3$  wherein  $R^3$  and  $R^4$  are as previously defined, and

(xx)  $=N-NR^4C(O)NR^5R^6$  wherein  $R^4$ ,  $R^5$  and  $R^6$  are as previously defined,

(8) cyclic substituents

(i) aryl, and optionally substituted aryl

(ii) heteroaryl, and optionally substituted heteroaryl

(iii) heterocycloalkyl, and optionally substituted heterocycloalkyl, and

(iv)  $C_3$ - $C_7$ -cycloalkyl, and optionally substituted  $C_3$ - $C_7$ -cycloalkyl, and

(9)  $C_1$  substituents with the exception of 10-methyl derivatives which are part of the above definitions under (1)

(i) -CHO

(ii) -CN

(iii)  $CO_2R^3$  wherein  $R^3$  is as previously defined

(iv)  $C(O)NR^5R^6$  wherein  $R^5$  and  $R^6$  are as previously defined

(v)  $C(S)NR^5R^6$  wherein  $R^5$  and  $R^6$  are as previously defined

(vi)  $C(NR^4)NR^5R^6$  wherein  $R^4$ ,  $R^5$  and  $R^6$  are as previously defined

(vii)  $CH=N-O-R^4$  wherein  $R^4$  is as previously defined

(viii)  $CH=N-R^4$  wherein  $R^4$  is as previously defined

(ix)  $CH=N-NR^7R^8$  wherein  $R^7$  and  $R^8$  are as previously defined

(x)  $CH=N-NR^4C(O)R^3$  wherein  $R^3$  and  $R^4$  are as previously defined, and

(xi)  $CH=N-NR^4C(O)NR^5R^6$  wherein  $R^4$ ,  $R^5$  and  $R^6$  are as previously defined;

$R^1$  is selected from the group consisting of

(1) H

(2) methyl

(3) methyl substituted with one or more substituents selected from the group consisting of

(i) F

(ii) -CN

(iii)  $CO_2R^{11}$  where  $R^{11}$  is  $C_1$ - $C_3$ -alkyl or aryl substituted  $C_1$ - $C_3$ -alkyl, or heteroalkyl substituted  $C_1$ - $C_3$ -alkyl

(iv)  $-C(O)NR^5R^6$  wherein  $R^5$  and  $R^6$  are defined as previously

(v) aryl, and optionally substituted aryl, and

(vi) heteroaryl, and optionally substituted heteroaryl

(4)  $C_2$ - $C_{10}$ -alkyl

(5) substituted  $C_2$ - $C_{10}$ -alkyl with one or more substituents selected from the group consisting of

(i) halogen,

- (ii)  $\text{OR}^4$  where  $\text{R}^4$  is defined as previously
- (iii)  $\text{C}_1\text{-C}_3\text{-alkoxy-C}_1\text{-C}_3\text{-alkoxy}$
- (iv)  $\text{-CHO}$
- (v)  $\text{oxo}$
- (vi)  $\text{NR}^7\text{R}^8$  wherein  $\text{R}^7$  and  $\text{R}^8$  are as previously defined
- (vii)  $=\text{N-O-R}^4$  where  $\text{R}^4$  is as previously defined
- (viii)  $\text{-CN}$
- (ix)  $-\text{S(O)}_n\text{R}^3$  where  $n = 0, 1, \text{ or } 2$  and  $\text{R}^3$  is as previously defined
- (x) aryl, and optionally substituted aryl
- (xi) heteroaryl, and optionally substituted heteroaryl
- (xii)  $\text{C}_3\text{-C}_8\text{-cycloalkyl}$ , and optionally substituted  $\text{C}_3\text{-C}_8\text{-cycloalkyl}$
- (xiii)  $\text{C}_1\text{-C}_{12}\text{-alkyl}$  substituted with heteroaryl, and optionally substituted heteroaryl
- (xiv) heterocycloalkyl
- (xv)  $\text{NHC(O)R}^3$  where  $\text{R}^3$  is as previously defined
- (xvi)  $\text{NHC(O)NR}^5\text{R}^6$  where  $\text{R}^5$  and  $\text{R}^6$  are as previously defined
- (xvii)  $=\text{N-NR}^7\text{R}^8$  wherein  $\text{R}^7$  and  $\text{R}^8$  are as previously defined
- (xviii)  $=\text{N-R}^4$  wherein  $\text{R}^4$  as previously defined, and
- (xix)  $=\text{N-NHC(O)R}^3$  wherein  $\text{R}^3$  is as previously defined,
- (4)  $\text{C}_1\text{-C}_{10}\text{-alkenyl}$  substituted with one or more substituents selected from the group consisting of
  - (i) halogen,
  - (ii)  $\text{OR}^4$  where  $\text{R}^4$  is as previously defined
  - (iii)  $\text{-CHO}$
  - (iv)  $\text{oxo}$
  - (v)  $-\text{S(O)}_n\text{R}^3$  where  $n$  and  $\text{R}^3$  are as previously defined
  - (vi)  $\text{-CN}$
  - (vii)  $-\text{CO}_2\text{R}^3$  where  $\text{R}^3$  is as previously defined
  - (viii)  $\text{NR}^7\text{R}^8$  wherein  $\text{R}^7$  and  $\text{R}^8$  are as previously defined
  - (ix)  $=\text{N-O-R}^4$  where  $\text{R}^4$  is as previously defined
  - (x)  $-\text{C(O)-R}^4$  where  $\text{R}^4$  is as previously defined
  - (xi)  $-\text{C(O)NR}^5\text{R}^6$  wherein  $\text{R}^5$  and  $\text{R}^6$  are as previously defined
  - (xii) aryl, and optionally substituted aryl
  - (xiii) heteroaryl, and optionally substituted heteroaryl
  - (xiv)  $\text{C}_3\text{-C}_7\text{-cycloalkyl}$
  - (xv)  $\text{C}_1\text{-C}_{12}\text{-alkyl}$  substituted with heteroaryl
  - (xvi)  $\text{NHC(O)R}^3$  where  $\text{R}^3$  is as previously defined

- (xvii)  $\text{NHC(O)NR}^5\text{R}^6$  where  $\text{R}^5$  and  $\text{R}^6$  are as previously defined  
 (xviii)  $=\text{N-NR}^7\text{R}^8$  wherein  $\text{R}^7$  and  $\text{R}^8$  are as previously defined  
 (xix)  $=\text{N-R}^4$  wherein  $\text{R}^4$  is as previously defined,  
 (xx)  $=\text{N-NHC(O)R}^3$  wherein  $\text{R}^3$  is as previously defined, and  
 (xxi)  $=\text{N-NHC(O)NR}^5\text{R}^6$  wherein  $\text{R}^5$  and  $\text{R}^6$  are as previously defined,

(5)  $\text{C}_2\text{-C}_{10}$ -alkynyl, and

(6)  $\text{C}_2\text{-C}_{10}$ -alkynyl substituted with one or more substituents selected from the group consisting of

(i) halogen,

(ii)  $\text{OR}^4$  where  $\text{R}^4$  is defined as previously

(iii)-CHO

(iv) oxo

(v)  $-\text{CO}_2\text{R}^3$  where  $\text{R}^3$  is as previously defined

(vi)  $-\text{C(O)NR}^5\text{R}^6$  wherein  $\text{R}^5$  and  $\text{R}^6$  are as previously defined

(vii) -CN

(viii)  $\text{NR}^7\text{R}^8$  wherein  $\text{R}^7$  and  $\text{R}^8$  are as previously defined

(ix)  $=\text{N-O-R}^4$  where  $\text{R}^4$  is as previously defined

(x)  $-\text{S(O)}_n\text{R}^3$  where  $n$  and  $\text{R}^3$  are as previously defined

(xi) aryl, and optionally substituted aryl

(xii) heteroaryl, and optionally substituted heteroaryl

(xiii)  $\text{C}_3\text{-C}_7$ -cycloalkyl

(xiv)  $\text{C}_1\text{-C}_{12}$ -alkyl substituted with heteroaryl

(xv)  $\text{NHC(O)R}^3$  where  $\text{R}^3$  is as previously defined

(xvi)  $\text{NHC(O)NR}^5\text{R}^6$  where  $\text{R}^5$  and  $\text{R}^6$  are as previously defined

(xvii)  $=\text{N-NR}^7\text{R}^8$  wherein  $\text{R}^7$  and  $\text{R}^8$  are as previously defined

(xviii)  $=\text{N-R}^4$  wherein  $\text{R}^4$  is as previously defined

(xix)  $=\text{N-NHC(O)R}^3$  wherein  $\text{R}^3$  is as previously defined, and

(xx)  $=\text{N-NHC(O)NR}^5\text{R}^6$  wherein  $\text{R}^5$  and  $\text{R}^6$  are as previously defined;

$\text{R}^2$  is selected from the group consisting of

(1) hydrogen

(2) OH

(3)  $\text{OR}^3$  where  $\text{R}^3$  is as previously defined

(4)  $\text{OC(O)R}^3$  where  $\text{R}^3$  is as previously defined, and

(5)  $\text{O(CO)OR}^3$  where  $\text{R}^3$  is as previously defined;

and X and Y taken together are selected from the group consisting of

(1) O



- (2)  $\text{NOR}^4$  wherein  $\text{R}^4$  is as defined previously
- (3)  $\text{N-O C(R}^9\text{)(CR}^{10}\text{)-O-R}^4$  where  $\text{R}^4$  is as previously defined and
  - (i)  $\text{R}^9$  and  $\text{R}^{10}$  are each independently defined as  $\text{R}^4$ , or
  - (ii)  $\text{R}^9$  and  $\text{R}^{10}$  are taken together with the atom to which they are attached form a  $\text{C}_3\text{-C}_{12}$  cycloalkyl ring,
- (4)  $\text{NR}^4$  wherein  $\text{R}^4$  is as previously defined, and
- (5)  $\text{N-NR}^7\text{R}^8$  wherein  $\text{R}^7$  and  $\text{R}^8$  are as previously defined, or one of X and Y is hydrogen and the other is selected from the group consisting of
  - (1)  $\text{-OR}^4$  wherein  $\text{R}^4$  is as previously defined, and
  - (2)  $\text{-NR}^7\text{R}^8$  wherein  $\text{R}^7$  and  $\text{R}^8$  are as previously defined.

$\text{R}^P$  is selected from the group consisting of

- (1) hydrogen
- (2)  $\text{R}^3$  as previously defined
- (3)  $\text{COR}^3$  where  $\text{R}^3$  is as previously defined;

subject to the proviso that when the structure is IV, Z and M are part of a five- or six- membered ring, said rings optionally being fully or partially unsaturated; for the six- membered ring, the bonding between Z and M is through a carbonyl group; for the five- membered ring, the bonding is directly between Z and M excluding CO; Z and M are independently selected from the group consisting of carbon, oxygen or N; and when  $\text{M} = \text{N}$  a second bridge may exist between this nitrogen and the oxygen of the 12-OH group whereby either an additional annulated oxazole or oxazine ring constitutes part of the molecule; and subject to the proviso that when the structure is V, Z and M are part of a five- or six- membered ring, said rings optionally being fully saturated or fully or partially unsaturated; for the six-membered ring, the bonding between Z and M is through a carbonyl group; for the five-membered ring, the bonding is directly between Z and M excluding CO; Z and M are independently selected from the group consisting of carbon, oxygen or nitrogen; and when  $\text{M} = \text{N}$  a second bridge may exist between this nitrogen and the urethane nitrogen.

7. (Currently Amended) A pharmaceutical composition comprising an antibiotic 10-desmethyl macrolide of claim 1 and a pharmaceutical excipient.

8. (Cancelled)

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9. (Currently Amended) A method of treatment of a human or animal subject to combat bacterial infection thereof, which method comprises administering to said subject an antibiotic 10-desmethyl macrolide of claim 1.

10. (Currently Amended) A 6-protected-hydroxy-10-acetyloxymethyl-10,11-unsaturated macrolide analog.